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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,223	06/29/2005	Heinz Schneider	09600-00031-US	9409

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EXAMINER	
MCCORMICK, MELENIE LEE	
ART UNIT	**PAPER NUMBER**
1655	

DATE MAILED: 10/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/538,223	SCHNEIDER, HEINZ	
	Examiner	Art Unit	
	Melenie McCormick	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-11 and 16-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-11 and 16-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on ____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on 09/29/06 has been acknowledged.

Claims 3-11 and 16-22 are presented for examination on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-11 and 16-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Inanami et al. (Free Radic Res), Schnieider et al. (US 6,656,608) and Jerkic et al. (Nephr Dial Trans), and further in view of Wu et al. (J. Nutr.) for the reasons set forth in the previous office action and restated below.

Inanami et al. beneficially teach the protective effects of the green tea polyphenol (-) catechin against damage in the brain caused by ischemia in gerbils. Inanami et al. further teach that the compound is intended to be orally (gastrointestinally) administered prior to a reperfusion event (surgery)- see entire document including abstract and methods. Please note that theanine is one of the predominant amino acids present in green tea, and would intrinsically be present in an extract of green tea. Inanami et al. do not expressly teach that the composition further comprises glycine or at least one NO donor which is a substrate of NO synthetase.

Schneider et al. beneficially teach that glycine is useful in protecting against damage caused by ischemia reperfusion. Schneider et al. further beneficially teach that

a composition comprising glycine is intended to be administered orally (see e.g. col 5 line 66-col 6 line 2). Schneider et al. also further beneficially teach that the composition is intended as a pre-operative treatment (see e.g. col. 6 lines 21-23). Schneider et al. also disclose that the composition may additionally contain arginine (see e.g. claim 7).

Jerkic et al. beneficially teach the protective effects of L-arginine administration in rats prior to a surgical procedure which would result in reperfusion injury. Jerkic et al. further beneficially teach that L-arginine administration is through drinking water (gastrointestinal administration) prior to the surgery.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the green tea extract taught by Inanami et al. and the glycine and L-arginine taught by Schneider et al. and Jerkic et al., respectively, to obtain a composition which would be useful for treating preoperative patients to reduce the risk of post operative complications (such as the oxidative injury caused by ischemia reperfusion). Since it is well known in the art that the majority of damage resulting from ischemia reperfusion is related to oxidative stress, it would have been obvious to the skilled artisan to combine a well known antioxidant (green tea extract) with L-arginine, especially since, as evidenced by Wu et al., L-arginine is notoriously well recognized in the art to be the main precursor of nitric oxide which is a known mediator of reperfusion (see Wu et al.-e.g., page ,2628). Since it has also been shown that glycine may be useful as a treatment to protect against ischemia reperfusion (as disclosed by Schneider et al.), it would have been obvious to include this compound in composition which was to be used for the same purpose. The adjustment of particular

conventional working conditions (e.g. administering the composition to a patient at a certain time before or after surgery) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments filed 09/29/06 have been fully considered but they are not persuasive.

Applicants have summarized the references used in the previous Office Action. It should be noted that Applicants state "Inanami et al. discloses administration of (-) catechin from green tea to gerbils for two weeks prior to surgery to induce transient focal brain ischemia", which is not correct. As the title of the Inanami reference suggests, the reference teaches that oral administration of (-) catechin *protects* against ischemia reperfusion-induced neuronal cell death in the gerbil (see e.g. title and entire article).

Applicants argue that none of the cited references alone, or in any combination, disclose or suggest the method of amended claim 10 of averting or reducing the risk of postoperative complications wherein a composition comprising a) green tea extract and b) at least one NO donor which is a substrate of NO synthetase, and/or one precursor of

this NO donor is gastrointesinally administered to a surgical patient, wherein administration of the composition takes place less than 24 hours before a surgical procedure.

As previously stated, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the green tea extract taught by Inanami et al. and the glycine and L-arginine taught by Schneider et al. and Jerkic et al., respectively, to obtain a composition which would be useful for treating preoperative patients to reduce the risk of post operative complications (such as the oxidative injury caused by ischemia reperfusion). Since it is well known in the art that the majority of damage resulting from ischemia reperfusion is related to oxidative stress, it would have been obvious to the skilled artisan to combine a well known antioxidant (green tea extract) with L-arginine, especially since, as evidenced by Wu et al., L-arginine is notoriously well recognized in the art to be the main precursor of nitric oxide which is a known mediator of reperfusion (see Wu et al.-e.g., page, 2628). Since it has also been shown that glycine may be useful as a treatment to protect against ischemia reperfusion (as disclosed by Schneider et al.), it would have been obvious to include this compound in composition which was to be used for the same purpose.

Applicants argue that the references do not suggest administration of these compounds less than twenty- four hours before a surgical procedure and have amended the claims to recite this limitation. Though the cited references do not explicitly state that administration takes place less than twenty- four hours before a surgical procedure, they do encompass the limitation of administration 24 hours prior to

a surgical procedure. Inanami et al. beneficially teach that (-) catechin is administered from 2 weeks prior to ischemia until 1 week after (see e.g. Materials and Methods, first paragraph). Schneider et al. teach a pretreatment (with glycine and arginine) starting 3 to 6 days before surgery, and during said 3-6 day period (see e.g. col 7, lines 11-12). This would mean that administration takes place up until the time of surgery, which is less than 24 hours before the surgery. Wu et al. teach administration of arginine during a reperfusion event (see e.g. page 2628, second column, paragraph 2). One of ordinary skill in the art would have been motivated to judiciously adjust the particular time of administration of these compounds based upon the beneficial teachings of the references.

Applicants argue that Inanami et al. do not disclose the use of green tree extract to protect against ischemia reperfusion injury. This is not persuasive, as Inanami et al. do disclose (-) catechin to protect against ischemia reperfusion injury. Applicant's exhibit has been considered, however, it is well known in the art that (-) catechin is extracted from green tea and is therefore, a green tea extract. Furthermore, Inanami et al. specifically disclose that the (-) catechin is from green tea (see e.g. page 360 Materials and Methods, first paragraph). Consequently, Inanami et al. reads on the instant claims.

The rejection under 35 U.S.C. 103 (a) is therefore deemed proper and is thus maintained.

Applicant's new claim 22 has been considered, but is also rejected under 35 U.S.C. 103 (a), as it is unpatentable over Inanami et al. (Free Radic Res), Schnieider et

al. (US 6,656,608) and Jerkic et al. (Nephr Dial Trans), and further in view of Wu et al. (J. Nutr.) for the reasons stated above. Claim 22 is drawn to the method of claim 10 wherein the postoperative complications are ischemia reperfusion injury, which is specifically taught by the above cited references.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melenie McCormick whose telephone number is (571) 272-8037. The examiner can normally be reached on M-F 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CHRISTOPHER R. TATE
PRIMARY EXAMINER